

Current ACIP Postexposure Prophylaxis Recommendations

- Use IG as soon as possible
- Vaccine, if also recommended, can be given at the same time
- Need results of a clinical trial comparing vaccine and IG to determine if hepatitis A vaccine can be used without IG

ACIP Recommendations for Pre-Exposure Use of Hepatitis A Vaccine

- All children 12-23 months old
- Catch-up vaccination of older children in areas with existing programs
- Persons at increased risk
 - Travelers
 - Persons with chronic liver disease
 - Men who have sex with men
 - Illicit drug users

Randomized Clinical Noninferiority Trial

Summary of Findings

- Hepatitis A vaccine efficacy was similar to that of IG (noninferiority criteria was met)
 - Assuming 90% IG efficacy, point estimate of vaccine efficacy is 86%; 95% CI upper bound is 76%
 - Assuming 85% IG efficacy, point estimate of vaccine efficacy is 80%; 95% CI upper bound is 64%
- Risk of hepatitis A among vaccine recipients was never > 1.5% greater than among IG recipients
- Evidence that IG might attenuate clinical illness

Hepatitis A Vaccine Postexposure Rationale

- Vaccine offers a number of advantages over IG
 - Flexibility to use vaccine in some circumstances postexposure would be beneficial
- Not all populations were studied in postexposure clinical trial
 - Age > 40
 - Medical conditions (i.e., not “healthy”)
- Additional data not likely to be forthcoming

Rationale for Proposed Wording

Populations not studied in clinical trials

- Takes into account other available information
- Chronic liver disease and immunocompromised persons -- Preference for IG
 - Known to have poorer response to vaccine pre-exposure
 - Chronic liver disease patients have more severe outcomes
- Persons > 40 years or not “healthy” -- No data
 - Little information in pre-exposure literature on which to base a preference for IG

Hepatitis A Vaccine Postexposure Recommendations from Selected Countries

- Canada (2000): Vaccine without IG is preferred method of post-exposure prophylaxis
 - IG for infants and immunocompromised
- UK (2001)
 - Vaccine if exposure within previous 7 days
 - IG
 - Exposure more than 7 days ago
 - Age > 50 years, cirrhosis, chronic HBV or HCV infection
- France, Italy, Belgium (2000-2003)
 - Vaccine only

Hepatitis A Vaccine Postexposure Revised Draft Recommendation, Paragraph 1

Unvaccinated persons who recently have been exposed to HAV should receive a single dose of hepatitis A vaccine (at the age-appropriate dose for pre-exposure use) or IG (0.02 mL/kg) as soon as possible. The efficacy of IG or vaccine when administered > 2 weeks after exposure has not been established. For persons who receive vaccine, the second dose should be administered according to the licensed schedule to complete the series.



Hepatitis A Vaccine Postexposure

Revised Draft Recommendation, Paragraph 2

IG should be used for children < 12 months old, immunocompromised persons, persons who have been diagnosed with chronic liver disease and persons for whom vaccine is contraindicated. Persons administered IG for whom hepatitis A vaccine is also recommended should receive a dose of vaccine simultaneously with IG. The post-exposure efficacy of hepatitis A vaccine in persons < 2 years or > 40 years old and persons with medical conditions has not been studied.

Hepatitis A Vaccine Postexposure Trial Italy, 1997*

- Enrolled 212 household contacts (aged 1-40 years) of hospitalized hepatitis A cases
- Randomized to receive vaccine (GSK) within 8 days of symptom onset of index case, or no intervention
- Outcome – IgM positive as measured at day 14 or 45 post-vaccination
- Vaccine efficacy 79% (95% CI 7-95%)
 - Trial stopped when reached statistical significance
- Outcomes
 - 2 in vaccinated group, ages 10 and 11 years, asymptomatic with normal ALT's
 - 12 in no intervention group, aged 3-23 years, majority symptomatic with elevated ALT's

Other Considerations from Postexposure Study

- Time since exposure
 - Previous study cut off at 7 days postexposure
 - Results of current study largely removes theoretical concern about diminished vaccine efficacy with longer time since exposure
 - No difference between groups in time since exposure
 - Most interventions given fairly late in 2 week postexposure window
- Comparability of two US licensed vaccines
 - Considered equivalent for pre-exposure use
 - Few head-to-head comparisons
 - Percent seroconversion after one dose appears similar